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"Memory, hither come": Psychopharmacology of memory, and more.

In "Memory, hither come" William Blake plays upon the centrality of memory to human experience and links it to both emotion and melancholy (https://www.poetryfoundation.org/poems/43685/song-memory-hither-come). Indeed, memory has long been a subject of fascination for both poets and psychopharmacologists and also features prominently in many clinical disorders which are leading causes of disease burden (Fineberg et al, Journal of Psychopharmacology, 2013 Sep;27(9):761-70). In this edition of the Journal several studies focus on various aspects of memory and related domains of cognition in both preclinical and clinically relevant studies.

Thomas et al (991835) report a pre-registered randomized controlled experiment combining a single dose of the cognitive enhancer, modafinil, with brief mindfulness training. The rational for the study was that people with attentional deficits may be less likely to benefit from mindfulness and thus may benefit from simultaneous augmentation with a cognitive enhancer. However, although modafinil acutely mimicked the effects of brief mindfulness training on state mindfulness, it did not enhance the effects of this training. Livermore et al, (991571) examined the selective effects of serotonin on choices to gather more information and examined whether changes to information sampling would be observed following acute doses of serotonergic and catecholaminergic clinical treatments. Results using the antidepressant drugs citalopram and atomoxetine showed acute changes of serotonin activity by way of a single dose of citalopram (but not atomoxetine) alter information-seeking behaviour. These results are preliminary and were found in healthy volunteers but do provide scope for further research. Steudte-Schmiedgen et al (1001087) used hydrocortisone as an adjunct to brief cognitive-behavioural therapy for specific fears and report on endocrine and cognitive biomarkers as predictors of symptom improvement. Hydrocortisone administration boosted the success of exposure therapy for specific fear even with a low-level therapist involvement. Metz et al, (997100) examined the effects of hydrocortisone and yohimbine on selective attention to emotional cues. Specifically, they investigated the influence of the sympathetic nervous system and hypothalamus–pituitary–adrenal (HPA) axis activation on selective attention to affective facial stimuli. Only hydrocortisone administration led to an attentional bias away from sad faces. Future studies should investigate the effects reported in both these papers in major mood disorders as the HPA Axis has long been thought to play a pivotal role in both the cause and treatment of these illnesses (Young AH, Stress, Volume 7, Issue 4, December 2004, Pages 205-208). Feld et al, (1005627) report specific changes in sleep oscillations after blocking human metabotropic glutamate receptor 5 in the absence of altered memory function. Interestingly, their findings indicate that mGluR5-related plasticity is not essential for memory processing during sleep, even though mGlurR5 are strongly implicated in the regulation of the cardinal sleep oscillations.

Xiaoxiao et al (991576) report that intranasal oxytocin may help maintain romantic bonds by decreasing jealousy evoked by either imagined or real partner infidelity. The neuropeptide oxytocin may enhance the maintenance of social bonds and reduce couple conflict, although its influence on jealousy evoked by imagined or real infidelity has hitherto been unclear. This study investigated the effects of intranasal oxytocin on romantic jealousy in both males and females in imagined and real scenarios. Xiaoxiao et al report that oxytocin reduces the negative emotional impact of jealousy in established romantic partners evoked by imagined or real infidelity or exclusive social interactions with others thus providing further support for oxytocin's putative role in maintaining relationships. Ramakrishna et al (986418) report a study of a histamine 3 receptor inverse agonist as a potential treatment of cognitive disorders. Central histamine 3 (H3) receptors are a family of presynaptic auto and heteroreceptors. Blockade of the presynaptic H3 receptors activates the downstream pathway(s) involved in the processes of learning and memory, making it a potential therapeutic option for

ameliorating cognitive dysfunction. The histamine 3 receptor inverse agonist studied (Samelisant (SUVN-G3031) was found to have potential utility in the treatment of cognitive deficits associated with a hypocholinergic state. Tanqueiro et al (1008560) sought to characterise BDNF signalling and function in a preclinical rodent model relevant to schizophrenia induced by prolonged NMDA-R hypofunction. They found that sustained NMDA receptor hypofunction impairs brain-derived neurotropic factor (BDNF) signalling in the prefrontal cortex (PFC), but not in the hippocampus, and disturbs PFC-dependent cognition in mice which may contribute to the PFC-dependent cognitive deficits seen in the subchronic PCP model. Lootibashian et al, (1000762) investigated the effect of Crocin on memory deficits induced by total sleep deprivation (TSD) on BDNF, TrkB, and ERK levels in the hippocampus of male Wistar rats. The adverse effects of TSD on the level of proteins in the hippocampus may disrupt synaptic plasticity and transmission, inducing memory impairment. Additionally, the restoration effect of crocin on the decrease in proteins level may be involved in its improvement effect on memory performance. Peled-Avron et al, (996884) tested the effects of methylphenidate on orienting bias in healthy individuals. Methylphenidate decreased spatial orienting bias in an asymmetric manner.

To round off this edition of the Journal, we have three other papers on psychopharmacological topics of great interest. Chiappini et al (959615) report on Promethazine abuse according to European Medicines Agency (EMA) adverse drug reaction reports. Anecdotal promethazine misuse/abuse reports were confirmed by EMA data and promethazine misuse/abuse is a clear concern and is associated with drug-related fatalities. Lin et al, (1008576) utilised an LC-MS/MS method for assessing drug's activity at dopamine and serotonin transporters using transporter-transfected HEK293T cells. Betts et al, (972421) report pharmacological evidence of a cholinergic contribution to elevated impulsivity and risky decision making caused by adding win-paired cues to a rat gambling task suggesting that the deleterious effects of win-paired cues on decision-making and impulse control may result from elevated cholinergic tone. What are we to conclude as we reflect on these diverse findings? Perhaps we should return once more to Blake, ""The road of excess leads to the palace of wisdom...You never know what is enough until you know what is more than enough."